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Application of Near-Infrared Spectroscopy to Investigate Brain Activity: Clinical Research

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ABSTRACT

Near infrared spectroscopy has recently been used to measure changes of optical parameters (i.e., light absorption or scattering) of brain tissue. The fact that the equipment is generally compact, portable, noninvasive, and reasonably priced makes it ideal for clinical and nonclinical evaluation and monitoring of brain function. Clinical and nonclinical studies evaluating changes related to light absorption are discussed, with an emphasis on cerebral blood oxygenation (CBO) changes and hemodynamic responses while performing cognitive tasks. With respect to the clinical studies, the focus is on variations in patterns of oxygenated hemoglobin (Oxy-Hb), deoxygenated hemoglobin (Deoxy-Hb) and Total-Hb (sum of Oxy-Hb and Deoxy-Hb). The studies about clinical applications includes research we have conducted with older adults and aphasics. Implications regarding the use of NIRS for clinical purposes are considered.

KEYWORDS: Near-infrared spectroscopy, brain activation, cognition, language, cerebral blood flow,

1. INTRODUCTION

NIRS is an optical method to measure concentration changes of Oxy-Hb and Deoxy-Hb in cerebral vessels by means of the characteristic absorption spectra of hemoglobin in the near-infrared range. Changes in Total-Hb indicate blood volume changes and correlate with rCBF. Simultaneous measurements made with NIRS and PET demonstrated that neuronal activation during mental tasks results in changes in cerebral oxygenation and hemodynamics measured by NIRS that were consistent with PET results[1]

NIRS has been applied to the evaluation of cerebral blood oxygenation and hemodynamic changes in a variety of brain activation studies[1-5]. In general, brain activation is related to an increase in Oxy-Hb, no change or a slight decrease in Deoxy-Hb, and an increase in Total-Hb. However, some research has suggested that in clinical subjects "typical" response may be less prevalent and other types of responses may be more common or typical of the clinical condition[6] The studies discussed here address this issue as well as basic research related to cognitive activation.

2. NEAR-INFRARED SPECTROSCOPY EQUIPMENT

We measured cerebral blood oxygenation and hemodynamics with a NIRO-500 (Hamamatsu Photonics). Near-infrared light from laser diodes, wavelengths 775, 825, 850, and 904 nm) was directed at the head through a fiberoptic bundle ("optode"), and reflected light was collected in the receiving fiberoptic bundle and transmitted to a photomultiplier tube. With the use of an algorithm developed by Cope et al[7] , absolute concentration changes of Oxy-Hb, Deoxy-Hb, and Total-Hb were continuously analyzed by means of a computer interfaced with the apparatus. NIRS data are expressed in arbitrary units. If the differential pathlength factor of the adult head is assumed to be 5.9, which was determined by time-of-flight measurement of a picosecond-length optical pulse through the tissues, 1 arbitrary unit equals 1 μmol/L. The optical distance was 3 to 4 cm. With an optode distance of 4 cm, correlations of Oxy-Hb and Total-Hb measured by NIRS and rCBF measured by PET suggested that the reliable penetration depth of near-infrared light into brain tissue is about 1.3 cm[8]

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3. AGING STUDY

Brain activation studies using positron-emission tomography (PET) have shown a variety of age-related alterations in neuronal activity that may suggest connectivity changes or variations in activation patterns[9]. In this study, NIRS was used to evaluate age-related alterations in CBO changes during the performance of various cognitive tasks[10]. .An additional objective was to determine if CBO response patterns varied in relation to type of cognitive task. Although our aging study concerns normal adults, we consider aging a clinical topic because of the nature of brain changes that occur with aging.

3.1. Methods

Twenty-six normal adults participants performed cognitive tasks to evaluate changes between the young group (13; mean age ± SD, 28.8 ± 4.4) and the older group (13; 50.7 ± 8.0). The groups were equivalent in education, $P > 0.10$). Six different cognitive tasks requiring oral language were performed with each task varying in the types of cognitive ability being tested. Tasks included semantic verbal fluency, confrontational naming, forward digit span, backward digit span, counting, and reading. The evaluation included a rest period (5-10 minutes), followed by the cognitive performance.

Optodes were placed on the left forehead so that the center was at the Fp2 position of the international EEG 10-20 system, thus the NIRS measured CBO changes in the left prefrontal cortex, an area of the brain involved in language, executive function, and complex problem solving. Participants were seated and their eyes were open during the entire experiment.

3.2. Results

In many NIRS studies on neuronal activation with the use of NIRO-500, the values of NIRS parameters were compared among different individuals; however, in the present study, qualitative pattern analyses were performed rather than quantitative analyses to avoid possible problems related to changes of the pathlength factor during aging. Skull thickness, skin absorption, and scattering properties of underlying brain structures such as subarachnoid space through which light passes, may change during aging, and the anatomical changes might alter the pathlength factor.
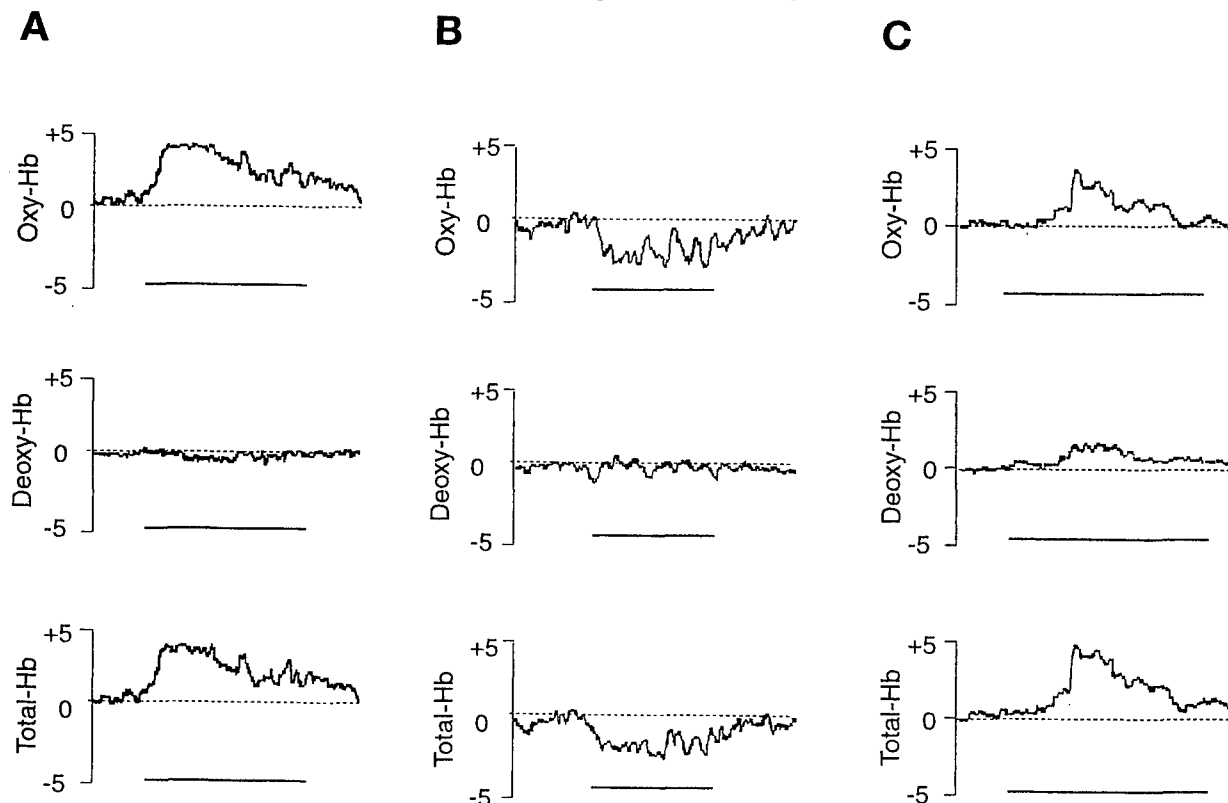

Figure 1. Examples of the three patterns: (A) the most common pattern, (B) the second most common patter, and (C) the thrid most common pattern.

The qualitative analyses consisted of determining the pattern of decrease and/or increase of the three NIRS parameters (Oxy-Hb, Deoxy-Hb, and Total-Hb), based on the maximum value from the preactivation baseline.

Each subject performed 6 cognitive tasks, making a total of 156 cognitive events. For the analyses, data from 3 subjects were deleted for the reading task and from 3 subjects for the counting tasks because of movement artifacts; therefore, a total of 150 events were evaluated.

The cognitive tasks altered CBO in the left prefrontal cortex of both young and older adults. To determine the types of response patterns, data for young and older subjects were combined. Most of the CBO changes could be classified into 3 patterns (Fig 1): Pattern A--Oxy-Hb and Total-Hb increased, Deoxy-Hb showed a little or no decrease; Pattern B--Oxy-Hb and Total-Hb increased, Deoxy-Hb shows little or no change; Pattern C--all three parameters increased.

Comparisons of the young and older group showed striking differences in the occurrence of the NIRS response patterns, as shown in Table 1. Although Pattern A was the most prevalent pattern in both groups, it occurred less often in the older group, P<0.01, In contrast, Pattern B, occurred more often in the older subjects than the young subjects, P <0.0001. Pattern C showed no age-related difference.

Table 1. Patterns of NIRS Parameter Changes Induced by Cognitive Tasks Performed by Young and Older Subjects

Pattern	Oxy, Deoxy, Tot	Young Group	Older Group
A "typical"	+, - ~ 0, +	**68.1%**	46.2%
B	-, - ~ 0 ~ +, +	6.9%	**34.6%**
C	+, +, +	9.7%	12.8%

Regarding specific tasks, age differences were evident verbal fluency and reading with the other tasks yielding no differences. Fig 2 shows the occurrence of the Patterns A and B induced by the tasks. In both tasks, Pattern A was more common for young subjects compared with the older subjects, and B was more common for the older subjects compared with the younger subjects. In the reading task, Pattern A occurred in 70% of the younger subjects; whereas, Pattern B was evident in 77% of the older subjects.
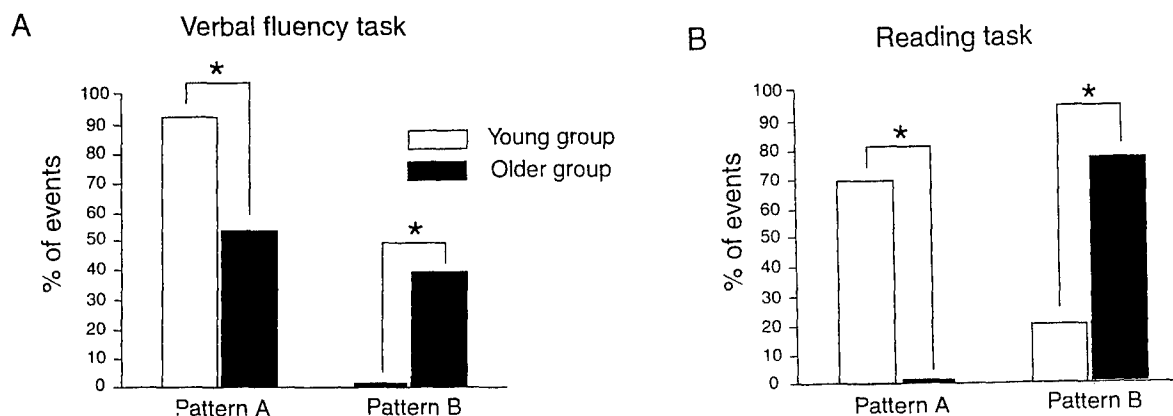

Figure 2. Comparison of the occurrence of the NIRS response patterns induced by the verbal fluency (A) and reading (B) tasks in the young and older groups.

3.3. Discussion

The study showed that cognitive tasks related to the frontal lobe caused various patterns of CBO responses in the left prefrontal cortex. The patterns of CBO responses were age-dependent and task-dependent. In both the young and older groups, the "typical" response of increases of Oxy-Hb and Total-Hb accompanied by a slight decrease or no change in

Deox-Hb was the most common pattern of NIRS parameter changes during the cognitive tasks (Pattern A). The NIRS parameter changes of Pattern A reflect an increase in rCBF at the measurement areas (6,8) The second most common pattern (Pattern B) has been observed in normal adults during cognitive tasks.

Although the "typical" pattern was most common for both young and older adults, it was less prevalent in the older group, and was evident in less than half the events. In the verbal fluency task, Pattern B was observed more in the older group than the young group. The results of the reading task are particularly intriguing in that almost all the older adults showed Pattern B, suggesting that for some types of tasks, rCBF response may change from an increasing response to a decreasing response during aging.

The results may reflect a possible functional reorganization during aging. Neuronal activities near the NIRS recording site may steal the blood flow at the NIRS measurement area, resulting in decreased rCBF. Other mechanism may also be involved, and further studies are necessary to clarify the physiological mechanism and roles of the rCBF decrease during neuronal activity.

This study demonstrates that NIRS can detect age-related changes in CBO and hemodynamics related to cognitive performance. NIRS has some advantages over PET and fMRI for brain activation studies, particularly related to aging. (1) PET images integrate CBO changes during task performance; in contrast, NIRS can monitor real-time (0.5 s) CBO changes during the tasks. Therefore, NIRS may be able to detect the neuronal activation that PET cannot image. (2) Compared with blood oxygenation level dependent (BOLD) ;contrast function MRI (fMRI), NIRS can measure changes of not only Deoxy-Hb but also Oxy-Hb and Total-Hb, which reflect CBF changes; whereas, BOLD fMRI detects only Deoxy-Hb changes. (3) The portability of the system makes investigations of the general population feasible.

It should be emphasized that the relatively small differences in age among subjects caused the age-related difference in CBO changes detected by NIRS, indicting that the age of subjects should be in narrow bands in NIRS cognitive studies.

4. NONFLUENT (BROCA'S) APHASIA STUDY

Aphasia is a disorder of language function that is one of the major symptoms caused by cerebrovascular disorder (CVD). We studied changes of cerebral blood oxygenation and hemodynamics induced by language activities in order to determine differences among nonfluent (Broca's) aphasic patients, normal subjects, and postroke non-aphasic patients[11] .

4.1. Methods

Three groups of age-matched subjects participated: nonfluent aphasics (n=10, mean age=56.9y), poststroke nonaphasic patients (n=6, mean age=52.5y), and normal controls (n=13, mean age=50.7y) performed a confrontational naming task, which is commonly included in aphasia test batteries. Methods were the same as those in the aging study.

4.2. Results

Analyses of the data are similar to the aging study, and as in the aging study, Patterns A, B, and C shown in Fig. 1 were the main patterns.

A summary of the occurrence of patterns appears in Table 2. Of note is the finding that the non-aphasic CVD patients and normal controls showed similar patterns; whereas, for the aphasic patients, Pattern C occurred most often. This pattern was evident in the normal and non-aphasic groups, but it was not as prevalent as it was in the aphasic patients.

Table 2 Patterns of NIRS Parameter Changes Induced by Naming Task in
Age-Matched Normal Adults, Non-Aphasic CVD Patients, and Aphasic Patients.

Pattern	Oxy, Deoxy, Tot	Age-matched Controls	Non-aphasic CVD Patients	Aphasic Patients
A "typical"	+, - ~ 0, +	39%	50%	30%
B	-, - ~ 0, -	31%	33%	0%
C	+, +, +	23%	17%	50%

Table 3 summarizes the mean changes of the NIRS parameters. Results of a one-way ANOVA comparing the performance of the 3 groups in the naming task demonstrated a significant effect for Deoxy-Hb, $F(2,27)=4.47$, $P < 0.05$, with aphasic patients differing significantly form normal subjects and nonaphasic CVD patients, while the 2 nonaphasic groups did not differ from each other. In contrast, there were no significant differences in Oxy-Hb or Total-Hb among the groups ($P > 0.05$).

Table 3. Mean ± SEM Changes of Oxy-Hb, Deoxy-Hb, and Total-Hb in
Age-Matched Control Subjects, Nonaphasic CVD Patients, and Aphasic Patients

Parameter	Age-Matched Controls	Nonaphasic CVD Patients	Aphasic Patients	p
Oxy-Hb	0.43±0.54	0.58±0.64	1.41±0.39	0.36
Deoxy-Hb	0.06±0.16[a]	-0.18±0.22[a]	0.78±0.29[b]	0.02
Total-Hb	0.48±0.58	0.39±0.71	2.19±0.40	0.08

NOTE: groups with similar letters did not differ

4.3. Discussion

In the aphasic patients with an increase of Deoxy-Hb, the rCBF in the left prefrontal cortex must be increased by the language task since both Oxy-Hb and Total-Hb were increased by the task, indicating the presence of coupling between rCBF and neuronal activity. However, the mean increase of Total-Hb in the aphasic patients was larger than that seen in normal subjects and nonaphasic CVD patients, suggesting that a larger increase of rCBF was induced by the language task in the aphasic patients. On the other hand, the increase of Deoxy-Hb indicates that the increase of oxygen consumption in the left prefrontal cortex of the aphasic patients was greater than that of nonaphasic patients. These observatons suggest that the left prefrontal cortex, in most of the aphasic patients, is more activated during language processing, resulting in more oxygen delivery and oxygen utilization compared with the nonaphasic patient group.

The advantages of NIRS with respect to PET and fMRI were discussed earlier in the Aging section. This study of aphasia confirms the need to consider oxygenation and deoxygenation when conducting clinical studies. In addition, the results of the quantitative one-way ANOVA highlights the value of doing qualitative analysis of NIRS parameter patterns as well as quantitative analyses. Although our analyses supported the finding about patterns, that all three parameters increased for the aphasic patients, it did not account for the fact that 50% of the aphasic patients had patterns that were not of this nature. The pattern of increases in all parameters is the most common pattern for the aphasics, but the sheer size of the response overrode the influence of other patterns. This should serve as a caveat, both for clinical researchers who focus only on quantitative data and to a tendency in some fields to assume that the nontypical response is artifactual or that subjects with nontypical responses should not be included in a study.

Because NIRS is portable and easy to use, it might be used to study recovery of function and CBO response after a stroke. For example patients who see the doctor could routinely be evaluated for CBO response induced by brain activation. The difficulties would relate to placement of the optodes and finding tasks that be given repeatedly without reduction in activation.

5. SUMMARY

To summarize, NIRS has shown that although normal adults show a "typical" pattern of increases in Oxy-Hb and Total-Hb, accompanied by a small or no decrease in Deoxy-Hb, there are a number of other patterns which should be considered and which may relate to neuronal loss or changes.

Regarding aging, older adults did not show the typical pattern as often as young adults. In addition, they tended to show a pattern of decreasing Oxy-Hb and Total-Hb with little or no change in Deoxy-Hb more often than young people. Concerning aphasics, the most common pattern was an increase in all three parameters which suggests excess oxygen utilization.

These issues call into question the use of pooled data for clinical groups without consideration of individual activation patterns. In addition, the fact that a person does not respond in the "typical" way does not mean the person is should be considered an outlier.

In spite of the low spatial resolution of contemporary NIRS equipment, it can be an important compliment to other brain activation research and diagnostic tools such as PET and fMRI. The temporal resolution surpasses PET, and the fact that oxygenation and deoxygenation changes means that NIRS offers information that cannot be obtained using fMRI. In addition, the portability and ease of use could make it a valuable tool in clinics, and perhaps for intensive care monitoring

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